

Remarks

Claims 1, 2 and 4 to 7 have been amended. Claims 12 and 42 have been cancelled without prejudice or disclaimer of the subject matter encompassed therein.

The amendment to claim 1 finds support in, *inter alia*, claim 1 as originally filed and paragraph [0007] of the published application. The amendments to claims 2 and 4 to 7 better conform the claim language to standard U.S. patent practice. Accordingly, Applicants submit that no new prohibited matter has been introduced by any of the claim amendments.

1. Examiner Teleconference

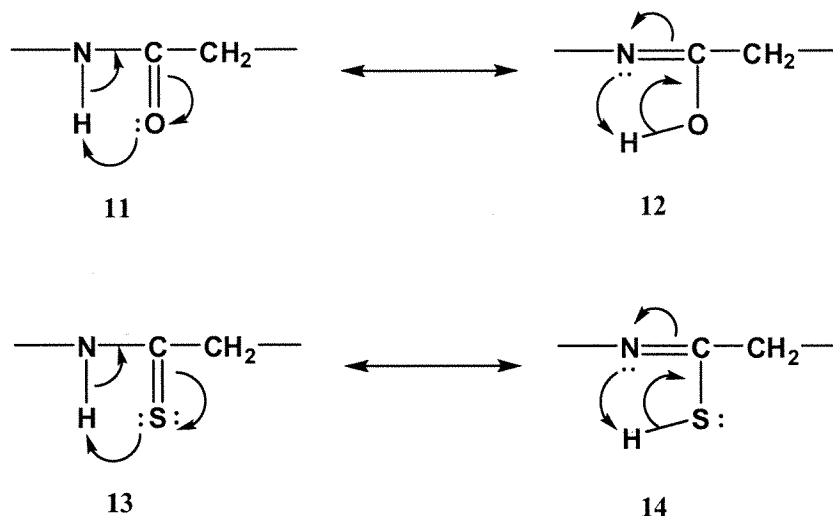
The undersigned and Applicants thank the Examiner for the teleconference on May 6, 2008, which clarified the objection to the claims as recited in the current Office Action. The details of the objection are discussed below in section 5.

2. Rejection under 35 U.S.C. 103(a)

Claims 1, 2, 4-7, 10, 12 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/21927 ("Coughlan") in view of Chem. Rev., 1996, 96(8), 3147-3176 ("Patani"). Specifically, the Examiner cites Example A23 in Coughlan and asserts that it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to substitute one of the carbonyl groups in the A23 compound with a thiocarbonyl group based on the teaching of Patani at page 3151.

Applicants submit that the cited section of Patani teaches the substitution of a hydroxyl group with a thiol group in an attempt to potentially provide a more clinically effect compound. The rationale for this substitution is provided on page 3151, lines 17-22 (left column) of Patani where it is stated that "the interchange of thiol for hydroxyl can be considered as an extension of the amino-hydroxyl replacement and has been used extensively in medicinal chemistry. This replacement is based on the ability of both these functional groups be hydrogen bond acceptors or donors."

The point is illustrated in Patani by Figure 8 on page 3151 where the different tautomeric forms of guanine and 6-thioguanine are shown.



Patani notes that “a mobile proton on a nitrogen atom in the aromatic ring can be transferred to the heteroatom [sulfur or oxygen] attached to the adjacent carbon resulting in the different tautomers”. Table 7 on page 3151 of Patani shows that the sulfur analog of a 1,4-dihydropyrimidine was more potent than the corresponding oxygen or amino analogs. Patani states that the ability of the sulfur atom to [internally] hydrogen bond was an important factor in retaining activity.

In contrast, Applicants’ claimed compounds do not possess a “mobile proton on a nitrogen” which can be transferred to the oxygen or sulfur atom attached to an adjacent carbon atom. Therefore, the possibility for generating the different tautomeric forms shown in Patani does not exist. Without Patani’s stated rationale for substituting sulfur for oxygen present, Applicants submit that Patani is not pertinent to the patentability of Applicants’ pending claims. Patani itself provides evidence of this statement since in a discussion of carbonyl group bioisosteres on pages 3166 to 3168, there is no teaching or suggestion of substituting a carbonyl group with a thiocarbonyl group.

Further, Coughlan states that the described 3-amino-4-arylmaleimides “are particularly potent and selective inhibitors of GSK-3” (page 4, lines 15-16). Given that replacement of the

one of the carbonyl oxygen atoms of these compounds with a sulfur atom would necessarily result in compounds that are larger (due to the larger van der Waal's radius of sulfur vs. oxygen), less electronegative (due to the decreased electronegativity of sulfur vs. oxygen) and more lipophilic, Applicants submit that such radical physicochemical changes would, in combination, likely have a negative impact on the observed potency and selectivity of the Coughlan compounds. Since Coughlan extols these features of the described maleimide compounds, Applicants submit that a person of ordinary skill in the art would have little reason to make such changes.

For at least the above-stated reasons, Applicants respectfully request that this rejection be withdrawn.

3. Rejection under 35 U.S.C. 112, first paragraph

Claims 1 to 5, 12 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Without acquiescing to the merits of the Examiner's rejection, Applicants have, in order to expedite allowance of the claims, cancelled claims 12 and 42 without prejudice or disclaimer of the subject matter encompassed therein and with the understanding that Applicants may pursue these cancelled claims in a continuation application. Without acquiescing to the merits of the Examiner's rejection regarding remaining claim 1 to 5, Applicants have amended these claims to conform to the scope of compounds as suggested by the Examiner on page 7 of the current Office Action.

Accordingly, Applicants respectfully submit that the amendment of claim 1 and the cancellation of claims 12 and 42 effectively overcome this rejection.

4. Obviousness-type Double Patenting

Claims 1, 2, 4 to 7, 9, 10, 12 and 42 are rejected as allegedly unpatentable over claims 1 to 9, 11 and 12 of copending Application No. 10/564,235. In particular, the Examiner asserts that the elected species of both applications are obvious variants.

Applicants submit that based at least on the discussion provided by Applicants in section 2 of this response, a compound containing a carbonyl group does not render obvious a corresponding compound containing a thiocarbonyl group. Clearly, Patani does not teach this substitution under a bioisosterism approach, and given the aforementioned significant physicochemical changes that would likely result from such a substitution, a person of ordinary skill in the art would not have a reasonable expectation of success in contemplating this action. Therefore, Applicants respectfully request that this rejection be withdrawn.

5. Objection to the Claims

Claims 1, 2, 4 to 7, 9, 10, 12 and 42 are objected to for allegedly reading on non-elected subject matter.

Based on a telephone conversation that the undersigned had with the Examiner on May 6, 2008, it is Applicants' understanding that this objection has been properly addressed by Applicants' submissions in section 2 of this response. In particular, Applicants submit that the scope of claim 1 should be expanded beyond that of the elected species due to the indicated novelty and unobviousness of the subject matter of claim 1 relative to the cited Coughlan and Patani references. The undersigned and Applicants thank the Examiner for his time and clarifying comments.


6. Conclusion

The foregoing amendments and remarks are being made to place the application in a condition for allowance. Applicant respectfully requests reconsideration and the timely allowance of the pending claims. Should the Examiner find that an interview would be helpful to further prosecution of this application, he is invited to telephone the undersigned at his convenience.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or to credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. 1.136(a)(3).

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